REMARKS

Reconsideration of the final rejection and/or objection to all claims is respectfully requested in view of the above amendments and the following remarks.

Claim Amendments

All pending claims have been presented above in accordance with the current Patent and Trademark Office procedures. The only current amendments are the amendment to claim 12 and the addition of new parallel method of treatment claim 13, as explained further below. As indicated above, claims 1, 2 and 8 are presented as previously amended and claims 4, 7 and 11 have been cancelled. Claims 3, 5, 6, 9 and 10 are as originally presented, except that claims 3, 6 and 9 have been reformatted to be consistent in presentation with the previously amended claims. Specifically, these claims have been reformatted by the use of block-indented paragraphs in a manner that is believed to make them easier to read, but the substance and wording of these claims is identical to the substance and wording of the like-numbered claims as originally filed in this application.

The amendment to method of treatment claim 12 and the addition of parallel method of treatment claim 13 have been made in the interest of expediting the allowance of these claims, or at least to place the method of treatment claims in better condition for appeal. These amendments are specifically directed to the section 112, 1st and 2nd paragraph grounds for rejection of previously examined claim 12, and reduce the scope of these claims. Therefore, no further examination is required. Entry of these amendments after final rejection is therefore believed to be in order and is respectfully requested.

Remaining Grounds for Rejection and/or Objection

At pages 2 and 3, the Examiner has conveniently summarized the disposition of the previous grounds for rejection, which is appreciated by the undersigned. The only remaining grounds for rejection, as understood, are:

- The rejection of claims 1-3, 5, 6, 9, 10 and 12 as being indefinite under section 112, 2nd paragraph with respect to the phrase "*in vivo* cleavable ester" recited in in claims 1, 6, 10 and 12; and
- The rejection of claim 12 as being indefinite under section 112, 2nd paragraph with respect to the phrase "a disease or medical condition mediated by a cytokine", and as not being enabled "for every 'disease or medical condition mediated by a cytokine,'" under section 112, 1st paragraph.

Section 112 Rejection Based on the Phrase "in vivo cleavable ester"

Claims 1-3, 5, 6, 9, 10 and 12 have been rejected under section 112, 2nd paragraph by reason of the recitation of "*in vivo* cleavable ester" in claims 1, 6, 10 and 12. The Examiner's asserted justification for this rejection appears to be essentially the same as in the Action mailed May 6, 2002. Applicants addressed each of these arguments point-by-point at pages 8 to 14 of their Amendment and Response thereto filed on November 6, 2002. Applicants continue to believe in the applicability and correctness of those arguments in overcoming this rejection, and urge the Examiner to reconsider those arguments together with the following comments.

The Examiner continues to assert that the "*in vivo* cleavable esters" lie outside of the subject matter of Formula I. This assertion is simply not understood. The "*in vivo* cleavable

ester" recited in claim 1 is just as much within the subject matter of Formula I as, for example, the optional substituents on Q, also recited in claim 1. Looked at from the other side, a compound that is of the structure of Formula I having each of the fixed and variable moieties set forth in claim 1, including an *in vivo* cleavable ester, would fall within the scope of this claim. Thus, infringement of such a claim does not depend on metabolism in the body to form an infringing compound. In fact, a meritorious purpose of including *in vivo* cleavable esters (or other prodrug components) as a part of the claimed structure is to directly address a reality of the pharmaceutical industry, whereby infringers attempt to avoid direct infringement by making often meaningless modifications to the active drug molecule, which "pop off" as soon as the drug is taken leaving the active moiety that was the subject of the claimed invention. The present claims specifically include this prodrug form within the scope of the claims, so that it is not necessary to rely on the body's metabolism to form the active drug, as might be the case with claims limited solely to the active drug.

As exhaustively explained in the previous November 6, 2002 remarks, there is ample guidance in this specification and in the cited literature with respect to the meaning of "*in vivo* cleavable ester" and, in any event, any person reasonably skilled in this art would well understand precisely what is meant by this recitation, and the phrase is not indefinite by any applicable standard applied by the Board or the courts.

The Examiner essentially dismisses without consideration the fact that recitations of prodrug moieties such as this are commonly included in patents allowed and issued by the

PTO.[1] The undersigned recognizes (and specifically acknowledged in the November 6, 2002 remarks) that the Examiner is not bound by what may have been done in another patent. But it is not understood how the Examiner can simply ignore the vast number of patent issuing with prodrug or the like recitations. The undersigned would like to believe that at least some effort is being made within the Patent and Trademark Office to achieve uniformity and consistent treatment of like issues between applications within the examining corps. Moreover, if there has been a policy change that supports the Examiner's departure from the well established norm, it would be appropriate for the Examiner to so inform applicants when making rejections such as this. The Examiner has not pointed to any change in policy that would justify the position he is maintaining in this application.

In view of the above considerations, it is respectfully requested that the Examiner reconsider and withdraw this ground for rejection.

Section 112 Rejection Based on the Phrase "a disease or medical condition mediated by a cytokine"

In a sincere effort to bring this application to allowance, claim 12 has been amended to change "cytokine" to "TNF," and claim 13 has been added to separately recite disease or medical conditions mediated by the production or effect of the interleukins IL-1, IL-6 or IL-8. Thus, it is believed that the Examiner's concern about the scope of the term "cytokine" has been addressed and overcome by more specifically reciting the mediating enzyme. Support for these specific mediating enzymes, and the inhibition thereof by compounds of this invention, is found in the specification, *inter alia*, at page 1, lines 7 to page 2, line 23, the

[1] Persons skilled in the art would understand from the specification and common knowledge in this art that "*in vivo* cleavable esters" of an active drug molecule are a type of "prodrug," so there is no need to specifically recite that characterization in the claims, contrary to the Examiner's suggestion.

assays disclosed beginning at page 44, line 11, and the disclosure at page 49, line 19 to page 51, page 19.

With these amendments, this ground for rejection is believed to have been overcome.

Conclusion

Entry of the above amendments is believed to appropriate after final rejection in that no further examination is require, they address a specific ground for rejection raised by the Examiner, and they are believed to place the claims in condition for allowance, or at least in better condition for appeal.

Reconsideration and withdrawal of all grounds for rejection, and allowance of all claims is respectfully requested in view of the above amendments and remarks.

Respectfully Submitted,
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